

Graft Biomechanics Following Three Corneal Transplantation Techniques

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Abstract

Purpose: To compare corneal biomechanical properties following three different transplantation techniques, including Descemet stripping automated endothelial keratoplasty (DSAEK), deep anterior lamellar keratoplasty (DALK) and penetrating keratoplasty (PK) in comparison to normal eyes.

Methods: This cross-sectional comparative study included 118 eyes: 17 eyes of 17 patients received DSAEK, 23 eyes of 21 patients underwent DALK using Anwar's big bubble technique, and 45 eyes of 36 patients had PK; 33 right eyes of 33 normal subjects served as the control group. Using the ocular response analyzer (ORA, Reichert Ophthalmic Instruments, Buffalo, New York, USA), corneal hysteresis (CH) and corneal resistance factor (CRF) were measured and compared among the study groups at least 3 months after all sutures were removed.

Results: Mean patient age was 26.9 ± 5.0 years in the control group, 28.8 ± 4.2 in the PK group, 27.2 ± 6.5 in the DALK group, and 62.5 ± 16.8 in the DSAEK group ($P < 0.001$). Central corneal thickness (CCT) was 539.0 ± 24.8 , 567.5 ± 38.8 , 547.0 ± 42.6 and 631.1 ± 84.8 μm , respectively ($P < 0.001$). CH and CRF were significantly lower in the DSAEK group (7.79 ± 2.0 and 7.88 ± 1.74 mmHg, respectively) as compared to the PK (10.23 ± 2.07 and 10.13 ± 2.22 mmHg, respectively) and DALK (9.64 ± 2.07 and 9.36 ± 2.09 mmHg, respectively) groups. The two latter groups demonstrated biomechanical parameters comparable to normal subjects (9.84 ± 1.59 and 9.89 ± 1.73 mmHg, respectively).

Conclusion: Graft biomechanical parameters after DSAEK are lower than those following PK and DALK. After PK and DALK in keratoconic eyes, these metrics are increased to normal values. These differences may have implications for interpreting intraocular pressure or planning graft refractive surgery after keratoplasty.

Keywords: Corneal Hysteresis; Corneal Resistance Factor; Deep Anterior Lamellar Keratoplasty; Descemet Stripping Automated Endothelial Keratoplasty; Penetrating Keratoplasty

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INTRODUCTION

Penetrating keratoplasty (PK) is not the grafting procedure of choice for all corneal disorders. Along with recent developments in corneal transplantation, selective replacement of the diseased corneal layer is performed. Nowadays, the trend is to perform

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deep anterior lamellar keratoplasty (DALK) for corneal pathologies not affecting the endothelium and Descemet's membrane (DM),^[1,2] and Descemet stripping automated endothelial keratoplasty (DSAEK) for patients with only endothelial dysfunction.^[3] This selective approach significantly eliminates complications occurring after full thickness PK. For instance, high postoperative astigmatism and the risk of traumatic wound dehiscence are decreased by DSAEK, and endothelial graft rejection is never observed after DALK.

However, none of these techniques are completely safe and complication-free. Post-keratoplasty refractive errors are encountered equally after both DALK and PK.^[4-6] In addition, increased corneal thickness after DSAEK can negatively impact the accuracy of intraocular pressure (IOP) measurements.^[7]

In order to surgically reduce post-keratoplasty refractive errors and compensate for inaccuracy in IOP readings, it is of great importance to understand biomechanical properties of a transplanted cornea, which seems to be different among PK, DALK and DSAEK for several reasons. First, DM removal from the donor cornea in DALK and of the recipient cornea in DSAEK can reduce corneal rigidity as compared to PK. Second, in PK, the healing response occurs at three layers between donor and recipient tissues including Bowman layer, corneal stroma and DM. However, there is no adhesion at the level of DM after DALK and the circumferential scar observed following PK and DALK, is totally absent after DSAEK. Third, some healing responses may occur at the recipient-donor interface which can influence biomechanical properties of DALK and DSAEK grafts as a whole. Finally, in contrast to PK and DALK in which the abnormal tissue is replaced by a normal matched cornea, DSAEK is an additive procedure where a donor lenticule of about 150 μm is added to the host cornea, resulting in a significant increase in corneal thickness.

The Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Buffalo, New York, USA) has made it possible to assess biomechanical properties of the human cornea in health and disease.^[8] It uses an air puff causing inward and then outward corneal motion from which two applanation measurements are calculated. Corneal hysteresis (CH), a measure of the viscoelastic properties of the cornea, is the difference between the inward and outward applanation pressures and attributed to corneal thickness and visco-elasticity.^[8] Corneal resistance factor (CRF) is another metric which is believed to be dominated by the elastic properties of the cornea and indicates its overall resistance.^[9]

The ORA has been used to evaluate biomechanics of corneal grafts after DSAEK,^[10] PK^[11] and DALK.^[12]

However, we are not aware of any study addressing possible biomechanical differences among these three distinct techniques of corneal transplantation. The aim of the present study was to compare biomechanical features of transplanted corneas following the above mentioned keratoplasty procedures using the ORA in comparison to a normal group.

METHODS

This cross-sectional comparative study included 118 eyes consisting of the following groups: PK, 45 eyes of 36 patients; DALK (Anwar's big bubble technique), 23 eyes of 21 patients; DSAEK, 17 eyes of 17 patients; control group, 33 normal right eyes of 33 refractive surgery candidates. The underlying pathology was keratoconus in the PK and DALK groups, and pseudophakic bullous keratopathy in the DSAEK group.

All participants had all sutures removed at least 3 months before entering the study. Exclusion criteria were the presence of ocular diseases other than the indication for keratoplasty, systemic disorders such as diabetes mellitus, history of additional ocular surgery such as re-grafting or refractive surgery of any kind, and the use of topical eye drops or contact lenses.

This study was approved by the Ethics Committee of the Ophthalmic Research Center at Shahid Beheshti University of Medical Sciences, Tehran, Iran and all participants provided written informed consent.

Surgical Technique

The technique of PK and DALK for keratoconus has previously been described in detail.^[2,4] In the DALK group, a bare DM was successfully achieved in all subjects. To perform DSAEK, the recipient epithelium was marked to outline where to strip DM and place the donor lenticule. A 5-mm superior scleral tunnel incision was made. The anterior chamber was filled with air and a reverse Sinsky hook was used to score DM in a circular pattern under the area of epithelial marking. DM and endothelium were stripped using a Descemet stripper. The donor lenticule was prepared using a Carriazo-Barraquer (CB)-microkeratome equipped with a 350 μm head (Moria Inc., Doylestown, PA, USA) and an artificial anterior chamber system (Moria Inc.). After dissection, the donor tissue was transferred to a punching system and cut with an 8.0 mm diameter trephine. A small amount of dispersive viscoelastic material (Coatel, Bausch and Lomb, Waterford, Ireland) was placed on the endothelial surface, and the disc was folded into a 60/40 taco-fold and introduced into the anterior chamber using forceps. The donor disc was unfolded and attached to the recipient corneal stroma using an air bubble. No corneal slits were performed in the eyes.

Ophthalmic Examinations and Measurements

An ocular examination including determination of uncorrected visual acuity (UCVA) and best spectacle-corrected visual acuity (BSCVA) using a Snellen acuity chart, slit lamp biomicroscopy, manifest refraction and keratometry was performed. In order to measure corneal biomechanics using the ORA (Reichert Ophthalmic Instruments, Buffalo, New York, USA), the patients were seated and asked to keep their eyes widely open while fixating on a green target light at the center of red lights. After releasing the air puff, measured parameters were displayed on the monitor. For each patient, four consecutive readings with good quality and two distinct peaks were obtained and averaged after excluding the outliers.

The last examination was corneal pachymetry using an ultrasonic contact probe (A/B scan; Sonomed Inc., Lake Success, New York, USA) after instillation of topical tetracaine 0.5%. The probe was held perpendicular to the center of the cornea and five measurements within a range of ±2 µm were taken and averaged for statistical analysis. All examinations and measurements were performed by a single ophthalmologist.

Statistical Analysis

Data were analyzed using SPSS software (version 15; SPSS Inc., Chicago, IL, USA) and those with a normal distribution (age, spherical equivalent refraction and central corneal thickness [CCT]) were compared among the study groups using the one-way ANOVA test. All other continuous variables were compared using the Kruskal-Wallis test (non-parametric ANOVA) and when the difference was statistically significant, multiple comparisons were performed by Bonferroni method. Chi-Square test was used for qualitative variables. *P* values less than 0.05 were considered as statistically significant.

RESULTS

Demographic and refractive data of the study groups are detailed in Table 1. DSAEK subjects were significantly

older as compared to other study groups (*P* < 0.001); however, mean age was comparable in the PK, DALK and control groups (*P* = 0.06). Mean follow-up period was significantly longer in the PK group as compared to the DALK and DSAEK groups (both, *P* < 0.001). Similarly, participants in the DALK group were followed significantly longer than those in the DSAEK group (*P* = 0.01).

Table 1 compares the study groups in terms of postoperative spherical equivalent refractive error and CCT. As indicated, refractive error was significantly lower and CCT was significantly thicker in the DSAEK group as compared to the other study groups (all, *P* values < 0.001). However there was no significant difference among the PK, DALK and control groups in terms of spherical equivalent refractive error (*P* = 0.18) or CCT (*P* = 0.09).

Figure 1 shows the distribution of CH and CRF values among the study groups. Table 2 demonstrates that CH and CRF were significantly lower in the DSAEK group as compared to the other study groups. These parameters were comparable among the PK, DALK and control groups.

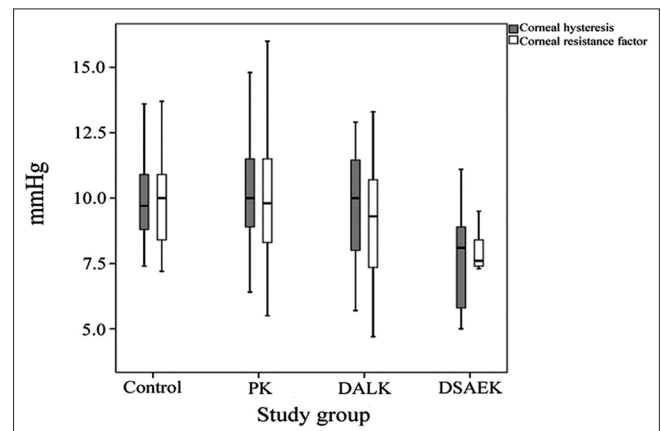


Figure 1. Comparison of corneal hysteresis and corneal resistance factor among the study groups. PK, penetrating keratoplasty; DALK, deep anterior lamellar keratoplasty; DSAEK, Descemet stripping automated endothelial keratoplasty.

Table 1. Characteristics of normal eyes and eyes undergoing PK, DALK, and DSAEK

Parameters	Control group (33 eyes)	PK group (45 eyes)	DALK group (23 eyes)	DSAEK group (17 eyes)	<i>P</i>
Age (years)	26.9±5.0 (20-40)	28.8±4.2 (16-46)	27.2±6.5 (17-44)	62.5±16.8 (51-80)	<0.001
Male/female ratio	16/17	31/14	13/10	9/8	0.31
OD/OS	33/0	21/24	14/9	5/12	<0.001
Follow-up period (months)	-	88.5±67.8 (17-296)	29.2±13.3 (18-52)	15.8±12.7 (6-67)	<0.001
Spherical equivalent refraction (D)	-3.25±1.34 (-6.75--1.25)	-2.87±2.78 (-11.5--2.25)	-4.11±3.46 (-12.5--1.25)	-0.80±2.26 (-6.5--2.0)	0.001
Central corneal thickness (µm)	539.0±24.8 (500-589)	567.5±38.8 (441-654)	547.0±42.6 (442-625)	631.1±84.8 (499-782)	<0.001

PK, penetrating keratoplasty; DALK, deep anterior lamellar keratoplasty; DSAEK, descemet stripping automated endothelial keratoplasty; OD, right eye; OS, left eye; D, diopter

Table 2. Corneal biomechanical metrics in normal eyes and eyes with prior PK, DALK, and DSAEK

Parameter (mmHg)	Mean±SD (range)				P			
	Control group	PK group	DALK group	DSAEK group	Control-DSAEK	PK-DSAEK	DALK-DSAEK	
Corneal hysteresis	9.84±1.5 (7.40-13.60)	10.23±2.07 (6.40-15.70)	9.64±2.07 (5.70-12.90)	7.79±2.0 (5.30-11.10)	0.002	0.02	0.001	0.041
Corneal resistance factor	9.89±1.73 (7.20-13.70)	10.13±2.22 (5.90-16.0)	9.36±2.09 (6.40-13.30)	7.88±1.74 (5.40-13.0)	0.001	0.004	0.001	0.03

SD, standard deviation; PK, penetrating keratoplasty; DALK, deep anterior lamellar keratoplasty; DSAEK, descemet stripping automated endothelial keratoplasty

DISCUSSION

The present study indicated that CH and CRF following PK and DALK in keratoconic eyes were comparable to those of normal age-matched control subjects. In sharp contrast, these metrics were significantly lower after DSAEK. This observation is in good agreement with the results of a study by John et al^[10] who reported that both CH and CRF were significantly lower after descemetorhexis with endokeratoplasty as compared to a normal age-matched group. They attributed this observation to the removal of the recipient DM and concluded that DM may act as a posterior pillar and contribute to the biomechanical properties of the normal cornea.

In addition to the above mentioned mechanism, other factors may be responsible for differences observed between the DSAEK and other groups in the current study. Three factors may contribute to changes in CH and CRF after corneal transplantation of any kind, including biomechanical characteristics of the transplanted corneal button, the healing response between donor and recipient corneas, and biomechanical characteristics of the residual recipient cornea.

The recipient stroma which remains in place after DSAEK can undergo alterations after a long period of edema. Histopathologic findings in corneas with bullous keratopathy have revealed the accumulation of extracellular matrix proteins including collagen and fibrillin-1 in the anterior stroma below the epithelium,^[13,14] as well as abnormal intrastromal deposits which were shown to be reduced significantly after DSAEK.^[15,16] However, some alterations may persist postoperatively and lead to reduced viscoelastic properties of the cornea. In DALK and PK, the stroma is completely replaced with a normal cornea which may improve corneal biomechanics in keratoconic eyes back to normal levels as was the case in our study.

Due to the differing indications for surgery, DSAEK subjects in our series were significantly older than other study subjects. It has been reported that aging is associated with a significant decrease in both CH and CRF^[17,18] which can also explain the observed differences between DSAEK and other groups. In order to better

understand the effect of aging on graft biomechanics, recipient age in the DSAEK group should be compared to donor age in the DALK and PK groups; however, this comparison was not possible in our study as there was no access to eye bank data in all subjects.

Another explanation for the observed lower metrics after DSAEK can be the absence of the circular scar between donors and recipients with this type of corneal transplantation. A ring scar develops between the donor and recipient corneas after DALK and PK which most probably contributes to graft biomechanics.

Central graft thickness was significantly greater in DSAEK eyes as compared to other study groups. It has been demonstrated that corneal biomechanics vary directly with CCT.^[19] It is possible that increased CCT in DSAEK eyes can partially compensate for the negative impacts of the above mentioned factors on CH and CRF. On the other hand, the relationship between corneal biomechanics and CCT in normal corneas may no longer be observed after corneal transplantation of any kind.

One striking observation of the current study is comparable CH and CRF following both PK and DALK, which were found to be similar to the normal group. It is well known that corneal biomechanical properties are reduced in keratoconus.^[20,21] The present study indicates that both DALK and PK can increase these metrics to normal levels. This is in contrast to the study by Yenerel et al^[11] which evaluated corneal biomechanics in different stages of keratoconus ranging from forme fruste to manifest keratoconus, as well as after PK and found significantly higher CH and CRF values in the PK group as compared to the keratoconus group. However, compared to the normal group, these values were significantly lower after PK. They concluded that although penetrating keratoplasty can improve corneal biomechanics in keratoconus, these characteristics do not return to normal levels. This difference between our study and Yenerel et al^[11] can be attributed to disparities such as trephination size and follow-up duration.

One limitation of the current study was that corneal biomechanics were not measured before keratoplasty. The results of the present study would have been more conclusive if measurements had also been performed before corneal transplantation. Thus, it could have

been determined the extent to which each technique of transplantation alters corneal biomechanics. Secondly, comparing ORA in different cases of corneal graft using various techniques and different underlying diseases makes it difficult to interpret the findings.

In summary, graft biomechanical properties after DSAEK are weaker than those after PK and DALK. The two latter techniques of corneal transplantation in keratoconic eyes can provide CH and CRF comparable to those in normal corneas. These differences in graft biomechanics should be considered in interpreting IOP measurements or planning graft refractive surgery after keratoplasty.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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